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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,636	02/25/2002	Ulrich Noth	00325-052901	3647

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EXAMINER

KAUSHAL, SUMESH

ART UNIT PAPER NUMBER

1636

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S.A.M.

**Office Action Summary****Application No.**

10/082,636

**Applicant(s)**

NOTH ET AL.

**Examiner**

Sumesh Kaushal Ph.D.

**Art Unit**

1636

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --****Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 17 March 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 February 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>111502</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

*This application claims priority under 35 USC 119 based upon U.S. Provisional Patent Application No. 60/270,977 filed on February 23, 2001.*

*Claims 1-9 are pending and are examined in this office action.*

*Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9305.*

### **Claim Rejections - 35 USC § 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 7-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Caplan et al (US 5,486,359 1996).

The instant claims are drawn to an isolated population of mesenchymal stem cells and a pharmaceutical composition thereof which can differentiate into cells of more than one connective tissue type (bone, cartilage, adipose, tendon, ligament and dermis) wherein the mesenchymal stem cells are obtained from bone (iliac crest or trabecular bone).

Caplan teaches therapeutic composition comprising an isolated homogeneous population of human mesenchymal stem cells, which can differentiate into cells of more

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than one connective tissue type (col. 35 claim 1; col. 37 claims 32-38). The cited art teaches that mesenchymal stem cells are the pluripotential blast cells found in bone marrow, blood, dermis and periosteum that are capable of differentiating into any of the specific types of mesenchymal or connective tissues (i.e. the tissues of the body that support the specialized elements; particularly adipose, osseous, cartilaginous, elastic, and fibrous connective tissues) see col.1 lines 22-34. The cited art further teaches that mesenchymal stem cells can be isolated from the bone marrow obtained from iliac crest, femora, tibiae, spine, rib or other medullary spaces. Bone marrow is the soft tissue occupying the medullary cavities of long bones, some haversian canals, and spaces between trabeculae of cancellous or spongy bone (col.2 lines 14-21; col.5, lines 10-20). Thus the cited art clearly anticipate the invention as claimed.

Claims 1, 5 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Gerson et al (US 5591625, 1997).

The instant claims are drawn to genetically engineered mesenchymal stem cells and a pharmaceutical composition thereof.

Gerson teaches isolated human mesenchymal stem cells, which can differentiate into more than one connective tissue type transfected with exogenous genetic material encoding a protein to be expressed. The cited art teaches the genetic modification of mesenchymal stem cells using a retroviral vector (col.18 lines 43-61; col.20 lines 15-21). In addition the cited art teaches that the scope of genetic modification of mesenchymal stem cells encompasses gene encoding cytokines to enhance

hematopoietic reconstitution and the cytokines that promotes repair and healing of injured bones (col. 8, lines 1-67; Col.9 lines 58-67). Thus the cited art clearly anticipate the invention as claimed.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gerson et al (US 5591625, 1997) as applied to claims 1,5 and 9 above, and further in view of Breibart et al (US 6077987, 2000).

The instant claims are drawn to genetically engineered mesenchymal stem cells, wherein the genetically engineered cells express a member of transforming growth factor- $\beta$  superfamily.

Gerson teaches isolated human mesenchymal stem cells, which can differentiate into more than one connective tissue type transfected with exogenous genetic material encoding a protein to be expressed. The cited art teaches the genetic modification of mesenchymal stem cells using a retroviral vector (col. 5-6, col.18 lines 43-61; col.20 lines 15-21). In addition the cited art teaches that the scope of genetic modification of mesenchymal stem cells encompasses cytokines to enhance hematopoietic

reconstitution and cytokines that promotes repair and healing of injured bones (col. 8, lines 1-67; Col.9 lines 58-67).

However Gerson does not specifically teach the genetic modification of mesenchymal stem cells to express a member of transforming growth factor- $\beta$  superfamily.

Breibart teaches genetic modification of mesenchymal cells to express a bioactive molecule selected from the group of TGF-b superfamily in order to promote wound healing, cell proliferation or differentiation in patients. The cited art further teaches that genetically modified mesenchymal cells are cartilage-forming cell that encodes a bioactive molecule selected from the group of TGF-beta superfamily consisting of bone morphogenic proteins (BMP), TGF-beta, and insulin-like growth factor (IGF). See col.6-7 sec.II, col.14 lines 37-67.

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the invention of Gerson who teaches genetic modification of mesenchymal stem cells with Breibart who specifically teaches genetic modification of mesenchymal cells with bone morphogenic proteins (BMP), TGF-beta, and insulin-like growth factor (IGF). One would have been motivated to do so because members of bioactive molecules belonging to TGF-beta superfamily are known to promote wound healing, cell proliferation and/or differentiation. One would have a reasonable expectation of success, since making genetic constructs expressing a bioactive molecule selected from TGF-beta superfamily and transduction of mesenchymal stem

cell using a viral or non-viral vectors has been routine in the art at the time of filing. Thus the invention as claimed is *prima facie* obvious in view of cited prior art of record.

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sumesh Kaushal  
Examiner Art Unit 1636

  
**JEFFREY FREDMAN**  
**PRIMARY EXAMINER**